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Clinical Study

Celiac disease in children with short stature: A hospital based study

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الملخص

أهداف البحث: لتحديد مدى انتشار حساسية القمح بين الأطفال قصار القامة. إن حساسية القمح مرض وراثي ناتج عن حساسية القمح " القلوتين " يؤدي إلى خلل في امتصاص الغذاء. ونسبة وقوعه عالمياً في إرتفاع. أجريت دراسة استعادية معتمدة على المستشفى في عيادة الغدد الصماء للأطفال في مستشفى الملك خالد الجامعي في الرياض.

طريقة البحث: تمت مراجعة ملفات الأطفال قصار القامة في الفترة ما بين يناير 1990 م وديسمبر 2009 م آخذين بالاعتبار التاريخ المرضي والفحص السريري وخاصية النمو، والفحص الشعاعي (عمر العظم) بالإضافة إلى تحليل الدم الروتيني وتحليل وظائف الغدة الدرقية. كما تم عمل فحوصات الكروموسومات عند اللزوم واستقصاء حساسية القمح مع أخذ عينة من الأمعاء عند اللزوم. كذلك تمت دراسة هرمونات النمو مع التحفيز عند الحاجة بالإضافة إلى فحص بالأشعة المغناطيسية للحالات الإيجابية.

النتائج: تم تقييم 110 من المرضى قصار القامة ممن تتراوح أعمارهم ما بين سنتين ونصف و 14 عاماً وذلك في الفترة المحددة للبحث وكانت نسبة الذكور للإناث هي 1.3 : 1. وكانت الوراثة هي السبب الشائع عند 51.8 % بينما كانت الأسباب مختلفة لدى 48.2 %. وكان من ضمنهم 5 مرضى (10 %) ممن لديهم حساسية القمح. مما يعني 4.5 % من جميع حالات قصر القامة.

الإستنتاجات: في هذه الدراسة ثبت أن حساسية القمح ليست بالنادرة. ولذا تعتبر حساسية القمح سبباً مهماً لقصر القامة ولأنها مرض صامت يتوجب عمل الفحوصات الاستقصائية اللازمة للأطفال قصيري القامة قبل دراسة هرمون النمو في حالات قصر القامة.

الكلمات المفتاحية: حساسية القمح; قصر القامة; أطفال; مضاد الندوميسيل; مضاد نسيج ترنس قلوتامينين; سعودي

Abstract

Objective: To identify the prevalence of celiac disease (CD) among children with short stature. Celiac disease (CD) is genetically determined gluten-sensitive enteropathy resulting in nutrient malabsorption, with an increasing incidence world-wide. A retrospective, hospital based study is conducted at a pediatric endocrine clinic, King Khalid University Hospital, Riyadh.

Methods: During the period between January 1990 and December 2009, the medical records of patients evaluated for short stature were reviewed. After a proper detailed history and physical examination, growth analysis, followed by radiological (bone age), and laboratory screening (CBC, and thyroid function) were performed. Celiac serological screening and chromosomal analysis were performed when appropriate, followed by small intestinal biopsy if indicated. Growth hormone stimulation test was performed in suspected patients, followed by magnetic resonance imaging (MRI) in positive cases.

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Results: Hundred and ten patients were evaluated for short stature over the period under review. Their age ranged from 2.6 to 14 years. The male to female ratio was 1.3:1. The commonest cause was genetic and found in approximately 51.8%, while in the other 48.2%, variable endocrine and non-endocrine causes were noted. Of the non-genetic short stature, 5 (10%) patients were found to have celiac disease, i.e. 4.5% of short children.

Conclusion: The prevalence of celiac disease is not rare in this study, therefore, celiac disease must be considered as an important cause of short stature. As, it could be a silent disease, it is recommended that a serological screening be done first to all patients before performing dynamic growth hormone testing in the evaluation of short stature.

Keywords: Anti-endomysial; Anti-tissue transglutaminase; Celiac disease; Children; Saudi; Short stature

Introduction

Celiac disease (CD) is a genetically determined disease, with permanent intolerance to ingested gluten that results in immunologically mediated inflammatory damage to the small intestinal mucosa. The prevalence of the disease in the general population is approximately 0.8%,[1] however, among children with short stature, the highest reported prevalence has been observed among Western Europeans and in countries to which Europeans emigrated, notably, North America and Australia.[2] In Brazil, the prevalence is reported to be 4.7%.[3] However, it is rare among people of purely African–Caribbean, Chinese, or Japanese background.[2]

In Arab countries CD is not that uncommon,[4] and limited studies on the prevalence of CD in children, especially those with short stature, showed a high prevalence of approximately 10%.[5–7]

Clinically infants with CD present with impaired growth, diarrhea, and abdominal distension. Usually atypical presentation is seen, who often, have no overt features of malabsorption. Extra intestinal manifestations such as short stature, delayed puberty, rickets, dental enamel defect, and arthralgia may occur as monosymptomatic manifestations.[8,9] The diagnosis of CD was based on clinical symptoms, positive serology sub as serum IgA-class, antireticulum, antigliadin and antiendomysial antibodies and a small bowel biopsy.[10–12] Histological evidence of CD was usually reported according to the Oberhuber classification.[13]

The pathogenesis of CD associated short stature is still unclear. Besides the involvement of the growth hormone/insulin-like growth factor-1 axis a role for ghrelin was recently proposed.[14,15]

The purpose of the present study is to determine the prevalence of CD among a group of short children, attending a pediatric endocrine clinic of King Khalid University Hospital (KKUH), King Saud University, Riyadh, Kingdom of Saudi Arabia, and highlights the importance of screening such children for celiac disease by anti-endomysial and anti-tissue transglutaminase antibodies before doing the time consuming dynamic growth hormone testing.

Materials and Methods

During the period between January 1990 and December 2009, children with short stature referred to a pediatric endocrine clinic, King Khalid University Hospital (KKUH), King Saud University (KSU), Riyadh, Kingdom of Saudi Arabia, were reviewed. After a proper detailed medical history, including nutritional history, parents' and siblings' height and age at puberty, birth weight, assessing the growth velocity and, complete physical examination, followed by radiological assessment including a bone age,[16] and appropriate laboratory screening (complete blood count, erythrocyte sedimentation rate, liver, renal and bone profiles and thyroid function) were done. A harbender stadiometer was used for height measurement. Chromosomal analysis was performed in the peripheral blood in females with otherwise unexplained short stature to rule out Turner's syndrome. In those patients with sub-normal growth velocity (growth velocity < 4 cm/year) dynamic growth hormone testing was performed following a standard procedure (one physiological and two biochemical testing).[17–20] Although, a random serum growth hormone value of more than 10 mg/dl generally exclude growth hormone deficiency (GHD), a random low serum growth hormone concentration does not confirm the diagnosis of GHD.[17–20] In patients with proved growth hormone deficiency, magnetic resonance of the pituitary (MRI) was performed. Celiac screening, for Celiac Disease was undertaken, using the endomysial antibodies in all short children with unexplained short stature, and confirmed by small biopsy if indicated.[10–13]

Results

During the period under review, January 1990 to December 2009, one hundred and ten patients with short stature were evaluated at a pediatric endocrine clinic, King Khalid University Hospital (KKUH), King Saud University (KSU), Riyadh, Kingdom of Saudi Arabia. Their age ranged between 2.6 and 14 years. The male to female ratio was 1.3:1. A wide spectrum of etiological causes of short stature was seen. Table 1 showed that the commonest form of short stature is genetic accounting for 51.8%. Various causes were noted (Table 2). Five patients in the non-genetic group were having positive serology for celiac disease, which were later confirmed by small bowel biopsy. Two of them were having other autoimmune disorders, i.e. one child was having diabetes and hypothyroidism while the other one was having type 1-polyglandular autoimmunity.

Table 1: Etiology of short stature in 110 children.

Cause	No. of patients	Percentage (%)
Genetic short stature	57	51.8
Familial short stature	53	
Constitutional growth delay	4	
Non-genetic short stature	53	48.2

Table 2: The non-genetic etiology among 110 children with short stature (53 children).

Aetiology	No. of patients	Percentage (%)
Idiopathic growth hormone deficiency	7	13.3
Primary hypothyroidism	6	11.5
Rickets/skeletal dysplasia	6	11.5
Celiac disease	5	9.5
Small for gestational age	5	9.5
Congenital adrenal hyperplasia	4	7.6
Dysmorphic child	4	7.6
Turner's syndrome	3	5.7
Laron dwarfism	2	3.8
Empty sella syndrome	2	3.8
Craniopharyngioma	2	3.8
Septo-optic-hypoplasia	2	3.8
Partial panhypopituitarism	2	3.8
Subarachnoid cyst	1	1.9
Histocytosis-X-	1	1.9
Pseudohypoparathyroidism	1	1.9

Discussion

Longitudinal growth assessment is essential in child care. Short stature can be promptly recognized only with accurate measurements of growth and critical analysis of growth chart. Short stature is defined as a standing height more than 2 standard deviations below the mean for sex and age (or below 3rd percentile).

The causes of short stature can be divided into three broad categories: genetic short stature (familial short stature, and constitutional delay of growth and development) chronic diseases including under nutrition, with its different causes, and endocrine diseases such as hypothyroidism, growth hormone secretion abnormalities, and excessive secretion of androgen as in congenital adrenal hyperplasia. Most short children evaluated by clinicians in developed countries have genetic short stature as shown in our series (51.8%). The hallmarks of genetic (familial) short stature include bone age appropriate for chronologic age, normal growth velocity, and predicted adult height appropriate to the familial pattern. By contrast, constitutional growth delay is characterized by delayed bone age, normal growth velocity, predicted adult height appropriate to the familial pattern, and delayed sexual maturation. Patients with constitutional growth delay typically have a first degree or second degree relative with constitutional growth delay and late puberty. This is in agreement with our study.[21,22]

This series shows a significant number of cases of CD (4.5%) among short Saudi children. The prevalence of CD in children with short stature has been studied in different regions of the world. In one study from Italy the prevalence of CD was found to be as high as 59%,[23,24] whereas it is estimated to be 4.7% in Brazil.[3] In Kingdom of Saudi Arabia, although limited studies, showed a prevalence of approximately 10%.[5–7] All children had no gastrointestinal symptoms. Screening for Celiac Disease is initiated with serological evaluation using IgA anti-tissue transglutaminase and IgA endomysial antibodies, with documentation of normal IgA levels. These tests have higher sensitivity and specificity than previously used anti-gliadin antibody tests.[12] Celiac Disease can lead to short stature by causing autoimmune hypothyroidism, resistance to growth hormone, and malabsorption of protein, calcium and vitamin D. Additionally, Celiac Disease can lead to hypogonadism which inhibits the pubertal growth spurt.[15] It is recommended by the American Diabetes Association Clinical Practice that antibody screening should be done in patients with type 1 diabetes.[25] Also, Down Syndrome has increased susceptibility to autoimmune diseases.[26] Patients with positive antibodies should be referred to a gastroenterologist for confirmation by small intestinal biopsy and to a dietitian for instruction on a gluten-free diet.

In conclusion, the prevalence of Celiac Disease is not rare in our community, in particular among children with short stature. Celiac Disease must be considered as an important cause and, therefore, should be screened for utilizing the available, simple, very sensitive and specific serological test which is much cheaper and less invasive than doing the dynamic growth hormone testing to start with.

Author contribution

N.A.M. Al Jurayyan: Idea, writing up the article and follow up of patients.
A.M.H. Al Nemri: Literature review and collecting data.
A.N.A. Al Jurayyan: Literature review and lab work.
A.M.A. Assiri: Performing the biopsy.

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